

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-55. (Canceled)

56. (Currently Amended) A method of ~~therapeutically~~ treating a patient having Alzheimer's disease in a patient, comprising administering to the patient an effective dosage of a pharmaceutical composition comprising a human, chimeric or humanized antibody that specifically binds to an epitope within residues 13-28 of A β and a pharmaceutical carrier, and thereby ~~therapeutically~~ treat the disease in the patient.

57. (Previously Presented) The method of claim 56, wherein the humanized antibody is a humanized version of the monoclonal antibody (ATCC accession number PTA-6123) for binding to A β .

58. (Previously Presented) The method of claim 56, wherein the antibody competes with the monoclonal antibody designated as 266 (ATCC accession number PTA-6123) for binding to A β .

59-60. (Canceled)

61. (Previously Presented) The method of claim 56, wherein the patient is a human.

62. (Canceled)

63. (Previously Presented) The method of claim 56, wherein the patient is under 50.

64. (Previously Presented) The method of claim 56, wherein the patient has inherited risk factors indicating susceptibility to Alzheimer's disease.

65. (Previously Presented) The method of claim 56, wherein the patient has no known risk factors for Alzheimer's disease.

66. (Previously Presented) The method of claim 56, wherein the antibody is a fragment of an intact antibody that competes with the intact antibody for specific binding to A β , and the antibody fragment is selected from the group consisting of Fab, Fab', F(ab')₂, Fabc, and Fv.

67-70. (Canceled)

71. (Previously Presented) The method of claim 56, wherein the antibody is a humanized antibody.

72. (Previously Presented) The method of claim 71, wherein the humanized antibody is an antibody fragment.

73. (Previously Presented) The method of claim 66, wherein the antibody is a humanized antibody.

74. (Previously Presented) The method of claim 56, wherein the antibody is a chimeric antibody.

75. (Previously Presented) The method of claim 74, wherein the chimeric antibody is an antibody fragment.

76. (Previously Presented) The method of claim 66, wherein the antibody is a chimeric antibody.

77. (Previously Presented) The method of claim 56, wherein the antibody is a bispecific antibody.

78. (Previously Presented) The method of claim 77, wherein the bispecific antibody is an antibody fragment.

79. (Previously Presented) The method of claim 66, wherein the antibody is a bispecific antibody.

80. (Canceled)

81. (Previously Presented) The method of claim 56, wherein the antibody is a polyclonal antibody.

82. (Canceled)

83. (Withdrawn) The method of claim 81, wherein the antibody is a rabbit antibody.

84. (Canceled)

85. (Currently Amended) The method of claim 56, wherein the isotype of the antibody is IgG1.

86. (Previously Presented) The method of claim 56, wherein a chain of the antibody is fused to a heterologous polypeptide.

87-91. (Canceled)

92. (Currently Amended) The method of claim 56, wherein the pharmaceutical composition~~agent~~ is administered intraperitoneally, orally, subcutaneously, intramuscularly, topically or intravenously.

93. (Currently Amended) The method of claim 56, wherein the pharmaceutical composition~~antibody~~ is administered in multiple dosages over a period of at least six months.

94. (Currently Amended) The method of claim 56, wherein the pharmaceutical composition~~antibody~~ is administered as a sustained release composition.

95-96. (Canceled)

97. (Currently Amended) A pharmaceutical composition comprising a ~~chimeric or human or~~ humanized antibody which specifically binds to an epitope within residues 13-28 of A β and a pharmaceutical carrier.

98. (Canceled)

99. (Currently Amended) The pharmaceutical composition of claim 97, wherein the humanized antibody is a humanized version of the monoclonal antibody 266 (ATCC accession number PTA-6123).

100. (Canceled)

101. (Withdrawn) A humanized antibody that specifically binds an epitope contained within positions 13-28 of A β .

102. (Withdrawn) A humanized antibody that binds to soluble A β .

103. (Withdrawn) A humanized antibody that sequesters A β peptide from its bound, circulating form in the blood, and alters clearance of soluble and bound forms of A β in central nervous system and plasma.

104. (Withdrawn) The humanized antibody of claims 101, 102, or 103 that is an intact humanized antibody.

105. (Withdrawn) The humanized antibody of claims 101, 102, or 103 that is a fragment.

106. (Withdrawn) The humanized antibody of claims 101, 102, or 103 that specifically binds to an epitope having an amino acid between positions 10-20, 10-25, 13-28, 15-20, or 20-30 of A β .

107. (Withdrawn) The humanized antibody of claims 101, 102, or 103 that specifically binds to an epitope within amino acid residues 10-20, 10-25, 13-28, 15-20, or 20-30 of A β .

108. (Withdrawn) The humanized antibody of claims 101, 102, or 103 that specifically binds to an epitope within amino acid residues 13-28 of A β .

109. (Withdrawn) The humanized antibody of claims 101, 102, or 103 that specifically binds to an epitope having an amino acid between positions 13-28 of A β .

110. (Withdrawn) The humanized antibody of claims 101, 102, or 103 that specifically binds to an epitope of A β to which antibody 266 binds.

111. (Withdrawn) The humanized antibody of claims 101, which specifically binds an epitope contained in positions 10-20, 13-28, or 15-20 of said A β peptide.

112. (Withdrawn) The humanized antibody of claim 111, which specifically binds an epitope that includes positions 15-20 of said A β peptide.

113. (Withdrawn) The humanized antibody of claim 111, which specifically binds an epitope that includes positions 16, 17 or 18 of said A β peptide.

114. (Withdrawn) The humanized antibody of claims 101, 102, or 103, which is a single chain antibody.

115. (Withdrawn) The humanized antibody of claims 101, 102, or 103, which comprises human framework regions.

116. (Withdrawn) The humanized antibody of claims 101, 102, or 103, which comprises CDR.

117. (Withdrawn) The humanized antibody of claims 101, 102, or 103, which is humanized Mab 266.

118. (Withdrawn) The humanized antibody, or fragment thereof, of claim 117, comprising a humanized light chain comprising the light chain complementarity determining regions (CDRs) from the mouse monoclonal antibody 266 and a light chain variable region framework sequence from a human immunoglobulin light chain; and a humanized heavy chain comprising the heavy chain CDRs from the mouse monoclonal antibody 266 and a heavy chain variable region framework sequence from a human immunoglobulin heavy chain.

119. (Withdrawn) An antibody fragment obtainable by enzymatic cleavage of the humanized antibody of any one of claims 101-118.

120. (Withdrawn) The fragment of claim 119 which is an Fab or F(ab')₂ fragment.

121. (Withdrawn) The fragment of claim 120, which is an F(ab')₂ fragment.

122. (Withdrawn) The fragment of claim 120, which is an F(ab')₂ fragment.

123. (Withdrawn) The humanized antibody or fragment of any one of claims 101-122 that is an IgG1 immunoglobulin isotype.

124. (Withdrawn) The humanized antibody or fragment of any one of claims 101-119, wherein the antibody or fragment thereof is produced in a host cell selected from the group consisting of a myeloma cell and a Chinese hamster ovary cell.

125. (Withdrawn) The humanized antibody or fragment of any one of claims 101-124, which is administered peripherally to a human subject, to exert its beneficial effects.

126. (Withdrawn) The humanized antibody or fragment of any one of claims 101-124, which, when administered peripherally to a human subject, does not need to cross the subject's blood-brain barrier to exert its beneficial effects.

127. (Withdrawn) The humanized antibody or fragment of any one of claims 101-124, which, when administered peripherally to a human subject, does not require cellular responses in the subject's brain to exert its beneficial effects.

128. (Withdrawn) The humanized antibody or fragment of any one of claims 101-124, which, when administered peripherally to a human subject, does not substantially bind aggregated A β in the subject's brain.

129. (Withdrawn) The humanized antibody or fragment of any one of claims 101-124, which, when administered peripherally to a human subject, exhibits beneficial effects without necessarily binding to A β plaques in the brain.

130. (Withdrawn) A nucleic acid, comprising a sequence coding for the light chain or the heavy chain of the humanized antibody of any one of claims 101-129, or a fragment thereof.

131. (Withdrawn) One or more nucleic acids, which when expressed in a suitable host cell, yield an antibody of any one of claims 101-129.

132. (Withdrawn) An expression vector for expressing the antibody or fragment of any one of claims 101-129 comprising nucleotide sequences encoding said antibody or fragment.

133. (Withdrawn) A cell transfected with the expression vector of claim 132.

134. (Withdrawn) A cell transfected with two expression vectors of claim 132, wherein a first vector comprises a nucleotide sequence encoding a light chain and a second vector comprises a nucleotide sequence encoding a heavy chain, wherein the first and second nucleotide sequences are components of the vector of claim 132.

135. (Withdrawn) A recombinant cell that produces the humanized antibody or fragment of any one of claims 117-118.

136. (Withdrawn) The cell of any one of claims 133-135, wherein the cell is selected from the group consisting of a myeloma cell, a Chinese hamster ovary cell and a Syrian hamster ovary cell.

137. (Withdrawn) A pharmaceutical composition that comprises the humanized antibody or fragment of any one of claims 101-129, and a pharmaceutically acceptable excipient.

138. (Withdrawn) A method to inhibit the formation of amyloid plaques in humans, comprising administering to a human subject in need or such inhibition an effective amount of a humanized antibody or fragment thereof that specifically immunoreacts with an epitope contained in positions 13-28 of A β .

139. (Withdrawn) A method to reduce amyloid plaques in humans, comprising administering to a human subject in need of such reduction an effective amount of a humanized antibody or fragment thereof which specifically immunoreacts with an epitope contained in positions 13-28 of A β .

140. (Withdrawn) A method to inhibit the formation of amyloid plaques in humans, comprising administering to a human subject in need of such inhibition an effective amount of a humanized antibody or fragment thereof that binds to soluble A β peptide.

141. (Withdrawn) A method to inhibit the formation of amyloid plaques in humans, comprising administering to a human subject in need of such inhibition an effective amount of a humanized antibody or fragment thereof that sequesters A β peptide from its bound, circulating form in blood.

142. (Withdrawn) A method to reduce amyloid plaques in humans, comprising administering to a human subject in need of such reduction an effective amount of a humanized antibody or fragment thereof which binds to soluble A β peptide.

143. (Withdrawn) A method to reduce amyloid plaques in humans, comprising administering to a human subject in need of such reduction an effective amount of a humanized

antibody or fragment thereof which sequesters A β peptide from its bound, circulating form in blood.

144. (Withdrawn) The method of any of claims 138-143, wherein said antibody or fragment, when administered peripherally to humans, does not need to cross the blood-brain barrier to inhibit the formation of amyloid plaques.

145. (Withdrawn) The method of claim 138 or claim 139, wherein said antibody or fragment, when administered peripherally to humans, does not elicit cellular responses to inhibit the formation of amyloid plaques.

146. (Withdrawn) The method of any of claims 138-143, wherein said antibody or fragment, when administered peripherally to humans, does not substantially bind aggregated A β in the brain.

147. (Withdrawn) The method of any one of claims 138-146, wherein the subject is diagnosed with clinical or pre-clinical Alzheimer's disease or Down's syndrome.

148. (Withdrawn) The method of any one of claims 138-146, wherein the subject is not diagnosed with clinical or pre-clinical Alzheimer's disease or Down's syndrome.

149. (Withdrawn) The method of any one of claims 138-139 or 144-148, wherein the antibody is administered by a peripheral route.

150. (Withdrawn) The method of claim 149, wherein the antibody is administered by an oral, intraperitoneal, subcutaneous, intramuscular, or intravenous route.

151. (Withdrawn) A method of reversing cognitive decline in a subject comprising administering to the subject an effective amount of a humanized antibody or fragment of any one of claims 101-129.

152. (Withdrawn) A method of improving cognition in a subject comprising administering to the subject an effective amount of a humanized antibody or fragment of any one of claims 101-129.

153. (Withdrawn) A method of treating cognitive decline in a subject comprising administering to the subject an effective amount of a humanized antibody or fragment of any one of claims 101-129.

154. (Withdrawn) A method of preventing cognitive decline in a subject comprising administering to the subject an effective amount of a humanized antibody or fragment of any one of claims 101-129.

155. (Withdrawn) The method of any one of claims 151-154, wherein said antibody or fragment is administered peripherally to humans.

156. (Withdrawn) The method of any one of claims 151-154, wherein said antibody or fragment, when administered peripherally to humans, does not need to cross the blood-brain barrier to affect cognition.

157. (Withdrawn) The method of any one of claims 151-154, wherein said antibody or fragment, when administered peripherally to humans, does not require cellular responses to affect cognition.

158. (Withdrawn) The method of any one of claims 151-154, wherein said antibody or fragment, when administered peripherally to humans, does not substantially bind aggregated A β in the brain.

159. (Withdrawn) The method of any one of claims 151-157, wherein the subject is diagnosed with clinical or pre-clinical Alzheimer's disease or Down's syndrome.

160. (Withdrawn) The method of any one of claims 151-157, wherein the subject is not diagnosed with clinical or pre-clinical Alzheimer's disease or Down's syndrome.

161. (Withdrawn) The method of any one of claims 151-160, wherein the antibody is administered by a peripheral route.

162. (Withdrawn) The method of claim 161, wherein the antibody is administered by an oral, intraperitoneal, subcutaneous, intramuscular, or intravenous route.

163. (Withdrawn) A method of treating Alzheimer's disease, comprising administering to a patient in need thereof an effective amount of the antibody or fragment of any one of claims 101-129.

164. (Previously Presented) The pharmaceutical composition of claim 97, which is a sustained release composition.

165. (Previously Presented) The pharmaceutical composition of claim 97, further comprising a physiologically acceptable diluent.

166. (Previously Presented) The pharmaceutical composition of claim 165 wherein the diluent is selected from the group consisting of distilled water physiological phosphate-buffered saline, Ringer's solution, dextrose solution, and Hank's solution.

167. (Previously Presented) The pharmaceutical composition of claim 166, wherein the diluent is physiological phosphate-buffered saline.

168. (Previously Presented) The pharmaceutical composition of claim 166, wherein the diluent is dextrose solution.

169. (Previously Presented) The pharmaceutical composition of claim 97, further comprising a macromolecule.

170. (Currently Amended) The pharmaceutical composition of claim 169, wherein the macromolecule is selected from the group consisting of proteins, polysaccharides

polysaccharides, polylactic acids, polyglycolic acids, copolymers, polymeric amino acids, amino acid copolymers, and lipid aggregates.

171. (Previously Presented) The pharmaceutical composition of claim 97, wherein the composition is suitable for parenteral administration.

172. (Previously Presented) The pharmaceutical composition of claim 97, wherein the carrier is a liquid carrier.

173. (Previously Presented) The pharmaceutical composition of claim 172, wherein the liquid carrier is selected from the group consisting of water, oil, saline, glycerol, and ethanol.

174. (Previously Presented) The pharmaceutical composition of claim 172, wherein the liquid carrier is propylene glycol.

175. (Previously Presented) The pharmaceutical composition of claim 172, wherein the liquid carrier is polyethylene glycol.

176. (Previously Presented) The pharmaceutical composition of claim 97, further comprising a wetting agent.

177. (Previously Presented) The pharmaceutical composition of claim 97, further comprising an emulsifying agent.

178. (Previously Presented) The pharmaceutical composition of claim 97, further comprising a surfactant.

179. (Previously Presented) The pharmaceutical composition of claim 97, further comprising a pH buffering substance.

180. (Previously Presented) The pharmaceutical composition of claim 97, wherein the pharmaceutical composition is a liquid solution.

181. (Previously Presented) The pharmaceutical composition of claim 97, wherein the pharmaceutical composition is a suspension.

182. (Previously Presented) The pharmaceutical composition of claim 97, which is a solid form suitable for solution in a liquid vehicle.

183. (Currently Amended) A method of ~~prophylactically treating~~ reducing risk or delaying onset of Alzheimer's disease in a patient at risk of the disease, comprising administering to the patient an effective dosage of a pharmaceutical composition comprising a human, chimeric or humanized antibody that specifically binds to an epitope within residues 13-28 of A β and a pharmaceutical carrier and thereby ~~prophylactically treat~~ reduce the risk or delaying the onset of the disease in the patient.

184. (Previously Presented) The method of claim 183, wherein the humanized antibody is a humanized version of the monoclonal antibody 266 (ATCC accession number PTA-6123).

185. (Previously Presented) The method of claim 183, wherein the antibody competes with the monoclonal antibody designated as 266 (ATCC accession number PTA-6123) for binding to A β .

186. (Previously Presented) The method of claim 183, wherein the patient is a human.

187. (Previously Presented) The method of claim 183, wherein the patient is asymptomatic.

188. (Previously Presented) The method of claim 183, wherein the patient is under 50.

189. (Previously Presented) The method of claim 183, wherein the patient has inherited risk factors indicating susceptibility to Alzheimer's disease.

190. (Previously Presented) The method of claim 183, wherein the patient has no known risk factors for Alzheimer's disease.

191. (Previously Presented) The method of claim 183, wherein the antibody is a fragment of an intact antibody that competes with the intact antibody for specific binding to A β , and the antibody fragment is selected from the group consisting of Fab, Fab', F(ab'), Fabc, and Fv.

192-193. (Canceled)

194. (Previously Presented) The method of claim 183, wherein the antibody is a humanized antibody.

195. (Currently Amended) The method of claim ~~183~~195, wherein the humanized antibody is an antibody fragment.

196. (Currently Amended) The method of claim ~~191~~192, wherein the antibody is a humanized antibody.

197. (Previously Presented) The method of claim 183, wherein the antibody is a chimeric antibody.

198. (Previously Presented) The method of claim 197, wherein the chimeric antibody is an antibody fragment.

199. (Previously Presented) The method of claim 191, wherein the antibody is a chimeric antibody.

200. (Previously Presented) The method of claim 183, wherein the antibody is a bispecific antibody.

201. (Previously Presented) The method of claim 200, wherein the bispecific antibody is an antibody fragment.

202. (Previously Presented) The method of claim 191, wherein the antibody is a bispecific antibody.

203. (Previously Presented) The method of claim 183, wherein the antibody is a polyclonal antibody.

204. (Previously Presented) The method of claim 183, wherein the isotype of the antibody is IgG1.

205. (Previously Presented) The method of claim 183, wherein a chain of the antibody is fused to a heterologous polypeptide.

206. (Canceled)

207. (Currently Amended) The method of claim 183, wherein the pharmaceutical composition~~agent~~ is administered intraperitoneally, orally, subcutaneously, intramuscularly, topically or intravenously.

208. (Currently Amended) The method of claim 183, wherein the pharmaceutical composition~~antibody~~ is administered in multiple dosages over a period of at least six months.

209. (Currently Amended) The method of claim 183, wherein the pharmaceutical composition~~antibody~~ is administered as a sustained release composition.